

07/03/001

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	955	424/93.21.ccls	USPAT; US-P GPUB	2003/03/05 15:48			0
2	BRS	L2	634	424/93.1.ccls.	USPAT; US-P GPUB	2003/03/05 15:48			0
3	BRS	L3	699	424/93.7.ccls.	USPAT; US-P GPUB	2003/03/05 15:49			0
4	BRS	L4	0	435/93.7.ccls.	USPAT; US-P GPUB	2003/03/05 15:49			0
5	BRS	L5	1982	1 or 2 or 3 or 4	USPAT; US-P GPUB	2003/03/05 15:49			0
6	BRS	L6	1938	myoblast	USPAT; US-P GPUB	2003/03/05 15:49			0
7	BRS	L7	204	5 and 6	USPAT; US-P GPUB	2003/03/05 15:49			0
8	BRS	L8	44744	cosmetic	USPAT; US-P GPUB	2003/03/05 15:49			0
9	BRS	L9	5	7 and 8	USPAT; US-P GPUB	2003/03/05 15:49			0

Set	Items	Description
S1	22338	MYOBLAST? ?
S2	27105	MYOGENIC
S3	6667	S2 (W) CELL? ?
S4	26958	S1 OR S3
S5	1927891	INJECT OR INJECTED OR INJECTION OR INJECTION
S6	1490	S4 AND S5
S7	1	AU="LAW, PETER K"
S8	3	AU="LAW PETER K"
S9	85	AU="LAW PK"
S10	30	AU="LAW P.K."
S11	119	S7 OR S8 OR S9 OR S10
S12	64	RD (unique items)
S13	53	S12 NOT PY>1993
S14	752	S6 NOT PY>1994
S15	407	RD (unique items)
S16	20	S15 AND (ADIPOCYTE? ? OR FAT)
S17	28203	CHONDROITIN(W) (SULFATE OR SULPHATE)
S18	2	S15 AND S17
S19	0	S15 AND COSMETIC
S20	378	S15 NOT (S11 OR S13 OR S16 OR S18)
?		

09/005,034 11/12/98 DIALOG

13/3/1 (Item 1 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07766285 93125036

Myoblast transfer therapy [letter]
Law PK
Lancet (ENGLAND) Jan 23 1993, 341 (8839) p247, ISSN 0140-6736
Journal Code: LOS
Languages: ENGLISH
Document type: LETTER

13/3/2 (Item 2 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07754120 94221387

Cell transplantation as an experimental treatment for Duchenne muscular dystrophy.
Law PK ; Goodwin TG; Fang Q; Deering MB; Duggirala V; Larkin C; Florendo JA; Kirby DS; Li HJ; Chen M; et al
Cell Therapy Research Foundation, Memphis, TN 38117.
Cell Transplant (UNITED STATES) Nov-Dec 1993, 2 (6) p485-505, ISSN 0963-6897 Journal Code: B02
Contract/Grant No.: NS 20251, NS, NINDS; NS 26185, NS, NINDS
Languages: ENGLISH
Document type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE II; JOURNAL ARTICLE

13/3/3 (Item 3 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07753132 94214800

Myoblast transplantation: setting the record straight [letter]
Law PK
Cell Transplant (UNITED STATES) Sep-Oct 1993, 2 (5) p437-8, ISSN 0963-6897 Journal Code: B02
Languages: ENGLISH
Document type: LETTER

13/3/4 (Item 4 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07311173 94199187

Feasibility, safety, and efficacy of myoblast transfer therapy on Duchenne muscular dystrophy boys.
Law PK ; Goodwin TG; Fang Q; Duggirala V; Larkin C; Florendo JA; Kirby DS; Deering MB; Li HJ; Chen M; et al
Cell Therapy Research Foundation, Memphis, TN 38117.
Cell Transplant (UNITED STATES) 1992, 1 (2-3) p235-44, ISSN 0963-6897
Journal Code: B02
Languages: ENGLISH
Document type: CLINICAL TRIAL; CLINICAL TRIAL, PHASE II; JOURNAL ARTICLE; MULTICENTER STUDY

13/3/5 (Item 5 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07311166 94199178

Dystrophin cytochemistry in mdx mouse muscles injected with labeled normal myoblasts.

Chen M; Li HJ; Fang Q; Goodwin TG; Florendo JA; Law PK
Cell Therapy Research Foundation, Memphis, TN 38117.
Cell Transplant (UNITED STATES) 1992, 1 (1) p17-22, ISSN 0963-6897
Journal Code: B02
Contract/Grant No.: NS 20251, NS, NINDS; NS 26185, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

13/3/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07157142 92410286
Myoblast transplantation [letter]
Law PK
Science (UNITED STATES) Sep 4 1992, 257 (5075) p1329; discussion
1329-30, ISSN 0036-8075 Journal Code: UJ7
Languages: ENGLISH
Document type: CLINICAL TRIAL; LETTER

13/3/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

06988837 90362936
Dystrophin production induced by myoblast transfer therapy in Duchenne muscular dystrophy [letter]
Law PK ; Bertorini TE; Goodwin TG; Chen M; Fang QW; Li HJ; Kirby DS;
Florendo JA; Herrod HG; Golden GS
Lancet (ENGLAND) Jul 14 1990, 336 (8707) p114-5, ISSN 0140-6736
Journal Code: LOS
Languages: ENGLISH
Document type: LETTER

13/3/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

06839839 92067498
Myoblast transfer therapy for Duchenne muscular dystrophy.
Law PK ; Goodwin TG; Fang QW; Chen M; Li HJ; Florendo JA; Kirby DS
Department of Neurology, University of Tennessee Memphis.
Acta Paediatr Jpn (JAPAN) Apr 1991, 33 (2) p206-15, ISSN 0374-5600
Journal Code: 1L3
Languages: ENGLISH
Document type: CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL

13/3/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

06511141 91063291
Myoblast transfer improves muscle genetics/structure/function and normalizes the behavior and life-span of dystrophic mice.
Law PK ; Goodwin TG; Li HJ; Ajamoughli G; Chen M
Department of Neurology, University of Tennessee, Memphis.
Adv Exp Med Biol (UNITED STATES) 1990, 280 p75-84; discussion 84-7,
ISSN 0065-2598 Journal Code: 2LU
Contract/Grant No.: NS-20251, NS, NINDS; NS-26185, NS, NINDS
Languages: ENGLISH
Document type: JOURNAL ARTICLE

13/3/11 (Item 11 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

06511128 91063277
Plausible structural/functional/behavioral/biochemical transformations following myoblast transfer therapy.
Law PK ; Goodwin TG; Li HJ; Chen M
Department of Neurology, University of Tennessee, Memphis.
Adv Exp Med Biol (UNITED STATES) 1990, 280 p241-9; discussion 249-50,
ISSN 0065-2598 Journal Code: 2LU
Contract/Grant No.: NS-20251, NS, NINDS; NS-26185, NS, NINDS
Languages: ENGLISH
Document type: CLINICAL TRIAL; JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

13/3/22 (Item 22 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

02701660 80032717
New muscle transplant method produces normal twitch tension in dystrophic muscle.
Law PK ; Yap JL
Muscle Nerve (UNITED STATES) Sep-Oct 1979, 2 (5) p356-63, ISSN
0148-639X Journal Code: NN9
Languages: ENGLISH
Document type: JOURNAL ARTICLE

13/3/25 (Item 25 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

02497622 78084587
Normal development of muscle fibers and motor end plates in dystrophic mice.
Burch TG; Law PK
Exp Neurol (UNITED STATES) Feb 1978, 58 (3) p570-4, ISSN 0014-4886
Journal Code: EQF
Languages: ENGLISH
Document type: JOURNAL ARTICLE

13/3/35 (Item 1 from file: 73)
DIALOG(R) File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

8744117 EMBASE No: 93048123
Myoblast transfer therapy (20)
Law P.K.
Cell Therapy Research Foundation, 1770 Moriah Woods Blyd, Memphis, TN
38117 USA
LANCET (United Kingdom) , 1993, 341/8839 (247)
CODEN: LANCA ISSN: 0140-6736 ADONIS ORDER NUMBER: 0140673693003340
LANGUAGES: English

13/3/36 (Item 2 from file: 73)
DIALOG(R) File 73:EMBASE
(c) 1998 Elsevier Science B.V. All rts. reserv.

8622413 EMBASE No: 92298751
Myoblast transplantation (1)
Law P.K. ; Furlong T.E.
Cell Therapy Research Foundation, 1770 Moriah Woods Boulevard, Memphis,

TN 38117 USA
SCIENCE (USA) , 1992, 257/5075 (1329-1330)
CODEN: SCIEA ISSN: 0036-8075
LANGUAGES: English

13/3/52 (Item 14 from file: 434)
DIALOG(R) File 434:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

01434110 Genuine Article#: CZ675 No. References: 23
**Title: MYOTROPIC INFLUENCES ON MOTONEURONS OF NORMAL AND DYSTROPHIC MICE IN
PARABIOSIS**
Author(s): LAW PK
Corporate Source: VANDERBILT UNIV,SCH MED,DEPT NEUROL/NASHVILLE//TN/37232;
VANDERBILT UNIV,SCH MED,JERRY LEWIS NEUROMUSCULAR
CTR/NASHVILLE//TN/37232; MCMASTER UNIV,MED CTR,DIV CLIN
NEUROSCI/HAMILTON 16/ONTARIO/CANADA/
Journal: EXPERIMENTAL NEUROLOGY, 1977, V54, N3, P444-452
Language: ENGLISH Document Type: ARTICLE
?

Set	Items	Description
S1	22338	MYOBLAST? ?
S2	27105	MYOGENIC
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S6	1490	S4 AND S5
S7	1	AU="LAW, PETER K"
S8	3	AU="LAW PETER K"
S9	85	AU="LAW PK"
S10	30	AU="LAW P.K."
S11	119	S7 OR S8 OR S9 OR S10
S12	64	RD (unique items)
S13	53	S12 NOT PY>1993
S14	752	S6 NOT PY>1994
S15	407	RD (unique items)
S16	20	S15 AND (ADIPOCYTE? ? OR FAT)
S17	28203	CHONDROITIN(W) (SULFATE OR SULPHATE)
S18	2	S15 AND S17
S19	0	S15 AND COSMETIC
S20	378	S15 NOT (S11 OR S13 OR S16 OR S18)

?t s20/3,ab/4,6,8,12,19,35,36,42,48,78,101,109,124,130,131,154,156,173,189,206,228,256,347

>>>No matching display code(s) found in file(s): 43, 129-130, 140, 158, 173, 187, 189, 376, 428-429, 441, 446, 449, 452-453, 455-456, 636

20/3,AB/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 1998 Dialog Corporation. All rts. reserv.

08188471 96050928

Gene complementation using myoblast transfer into fetal muscle.

Sopper MM; Hauschka SD; Hoffman E; Ontell M

Department of Cell Biology and Physiology, University of Pittsburgh School of Medicine, PA 15261, USA.

Gene Ther (ENGLAND) Mar 1994, 1 (2) p108-13, ISSN 0969-7128

Journal Code: CCE

Contract/Grant No.: AR36294, AR, NIAMS

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Gene complementation by **myoblast** transfer into neonatal or adult muscle has been proposed as a therapy for primary myopathies as well as to augment non-muscle gene products that may be diminished in the adult circulation. This paper describes a technique whereby **myoblasts** have been **injected** into limb muscles of normal and dystrophin-deficient (mdx) fetal mice (during the period of active myotube formation and prior to the development of the host's immune competence) without significantly interfering with fetal viability or further maturation. More mosaic myofibers (myofibers containing both host- and donor-derived myonuclei) appear to result from these transfers than have been reported following **myoblast** transfer into neonatal muscle or adult muscle. The small size of the fetal hosts' muscles and the lack of well-defined connective tissue septa facilitate migration of donor **myoblasts** into muscle groups distal to the **injection** site. The use of donor **myoblasts** derived from a tetraploid variant of a mouse **myogenic** cell line (MM14) provides a convenient and permanent cytological marker for the recognition of donor **myoblasts** and donor-derived myonuclei. When MM14 **myoblasts** are **injected** into mdx fetuses, whose muscles lack dystrophin, mosaic myofibers contain sufficient dystrophin to be visualized with routine immunohistochemical techniques. The **myoblast** transfer system, using fetal hosts, described in this study will facilitate the evaluation of **myoblasts** as vectors to overcome genetic deficiencies that may be manifested during fetal development.

20/3,AB/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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08089450 95102868

Gene therapy for muscle diseases.

Coover DD; Burghes AH

Ohio State University, Columbus.

Curr Opin Neurol (UNITED STATES) Oct 1994, 7 (5) p463-70, ISSN 1350-7540 Journal Code: BX4

Languages: ENGLISH

Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL

Duchenne muscular dystrophy involves progressive degeneration of the skeletal and cardiac muscles, resulting in premature death. A number of methods are currently being developed for the treatment of Duchenne muscular dystrophy and other neuromuscular disorders. A number of the viral vector systems, **myoblast** transfer, and direct **injection** techniques that are currently under investigation for the treatment of neuromuscular disorders are reviewed here.

20/3,AB/8 (Item 8 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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08039478 95035226

Gene transfer into skeletal muscles by isogenic myoblasts.

Huard J; Acsadi G; Jani A; Massie B; Karpati G

Montreal Neurological Institute, Quebec, Canada.

Hum Gene Ther (UNITED STATES) Aug 1994, 5 (8) p949-58, ISSN 1043-0342 Journal Code: A12

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The best way to overcome immunorejection in heterologous **myoblast** transfer (HMT) is by the use of immunodeficient and/or highly immunosuppressed mice as hosts. The same may be attained by autologous **myoblast** transfer (AMT). In this paper, we describe **myoblast** transfer in mdx and normal mice where the donor **myogenic cells** originated from highly inbred litter mates that are considered to be isogenic and thus the procedure is analogous to AMT. The **myoblasts** were marked in vitro with Rous Sarcoma Virus (RSV)-luciferase (Lux) or RSV-beta-galactosidase (LacZ) reporter genes through transduction mediated by an autonomously replication-defective recombinant human adenovirus. This permitted us to follow their fate after transplantation. mdx and normal mice were irradiated with 20 Gray gamma rays; necrosis and regeneration were induced by intramuscular notexin prior to **myoblast injection**. In both mdx and normal mice, the expression of luciferase rapidly declined after the **injection** implying that a large portion of the **injected myoblasts** were lost by 48 hr, due to undetermined cause(s). The surviving, **injected myoblasts** well-mosaicized large groups of host fibers but only in the immediate vicinity of the **injection**. Substantial expression of the reporter gene continued up to 1 month post-transplantation in normal mice, but there was a gradual decline and eventual disappearance of the reporter gene expression in mdx mice. This latter phenomenon was due to the ongoing intense necrosis of muscle fibers in mdx. There was no evidence of immunorejection. These experiments indicate that even in the absence of immunorejection, **myoblast** transfer suffers from important negative features: major loss of **myoblasts** within 48 hr after the **injection** and lack of significant spread of the **injected** cells from the **injection** site in the host muscle. These factors, plus the limited proliferative and fusion capacity of Duchenne muscular dystrophy (DMD) **myoblasts**, make them less than an ideal vector for the dystrophin cDNA for dystrophin gene replacement therapy in DMD.

20/3,AB/12 (Item 12 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07982412 94344183

Utilization of myoblasts from transgenic mice to evaluate the efficacy of myoblast transplantation.

Kinoshita I; Huard J; Tremblay JP

Laboratoire de Neurobiologie, Universite Laval, Hopital de l'Enfant-Jesus, Quebec, Canada.

Muscle Nerve (UNITED STATES) Sep 1994, 17 (9) p975-80, ISSN 0148-639X
Journal Code: NN9

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A possible treatment for Duchenne muscular dystrophy is the injection of normal **myoblasts** into dystrophic muscles to induce the formation of new, healthy, and dystrophin-positive muscle fibers. To develop this therapy, it is important to identify the muscle fibers formed by the **injected myoblasts** in the host muscles. In this study, we used **myoblasts** from transgenic mice which have a gene expressing beta-galactosidase under the control of the promoter of quail fast skeletal muscle troponin I. This transgene is expressed in myotubes and muscle fibers, but not in **myoblasts**. Twenty-eight days after **myoblast** transplantation in nude and in mdx mice, muscle fibers containing of beta-galactosidase were identified by x-gal staining. In mdx mice, most of the beta-galactosidase-positive muscle fibers resulting from the **myoblast** transplantation were also dystrophin positive. This technique could make it possible to follow the success of **myoblast** transplantation even in mice that are not depleted of dystrophin.

20/3,AB/19 (Item 19 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07869668 94157077

High efficiency of muscle regeneration after human myoblast clone transplantation in SCID mice.

Huard J; Verreault S; Roy R; Tremblay M; Tremblay JP

Centre de recherche en Neurobiologie, Hopital de l'Enfant-Jesus, Quebec, Canada.

J Clin Invest (UNITED STATES) Feb 1994, 93 (2) p586-99, ISSN 0021-9738
Journal Code: HS7

Languages: ENGLISH

Document type: JOURNAL ARTICLE

SCID mouse tibialis anterior muscles were first irradiated to prevent regeneration by host **myoblasts** and **injected** with notexin to damage the muscle fibers and trigger regeneration. The muscles were then **injected** with roughly 5 million human **myoblasts**. 1 mo later, 16-33% of the normal number of muscle fibers were present in the **injected** muscle, because of incomplete regeneration. However, > 90% of these muscle fibers contained human dystrophin. Some newly formed muscle fibers had an accumulation of human dystrophin and desmin on a part of their membrane. Such accumulations have been demonstrated at neuromuscular junctions before suggesting that the new muscle fibers are innervated and functional. The same pool of clones of human **myoblasts** produced only < or = 4% of muscle fibers containing human dystrophin when **injected** in nude mice muscles. Several of the human **myoblasts** did not fuse and remained in interstitial space or tightly associated with muscle fibers suggesting that some of them have formed satellite cells. Moreover, cultures of 98% pure human **myoblasts** were obtained from transplanted SCID muscles. In some mice where the muscle regeneration was not complete, the muscle fibers containing human dystrophin also expressed uniformly HLA class I, confirming that the fibers are of human origin. The presence of hybrid muscle fibers containing human dystrophin and mouse MHC was also demonstrated following transplantation. These results establish that in absence of an immune reaction, transplanted human **myoblasts** participate to the muscle regeneration with a high degree of efficacy even if the animals were killed only 1 mo after the transplantation.

20/3,AB/35 (Item 35 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07548919 93274510

Myoblast transfer therapy in the treatment of ptosis: a preliminary study.

Baker RS; Bonner PH; Porter JD; Madhat MN; Gross J

Department of Ophthalmology, University of Kentucky Medical Center, Lexington 40536-0284.

J Pediatr Ophthalmol Strabismus (UNITED STATES) Mar-Apr 1993, 30 (2) p113-7, ISSN 0191-3913 Journal Code: JMI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Congenital ptosis with poor levator function is now managed by frontalis suspension techniques. While this procedure is better than those used in the past, serious shortcomings exist. A technique producing more normal lid function would be a beneficial addition to surgical management. Since congenital ptosis is thought to be a focal myopathy, we investigated the potential of **myoblast** transfer therapy in myopathic levator palpebrae superioris. Satellite cells harvested from temporalis muscle were grown as clones, labeled with Dil, and transplanted into experimentally myopathic levator muscle of the same animal. Within 2 weeks, the **injected** cells were found to be incorporated into muscle fibers within the levator basal lamina. The control side appeared myopathic with very little muscle regeneration. The presence of Dil labeled muscle fibers in the experimental muscles strongly suggests their origin from the **injected** cells. Electron microscopy of nearby sections showed these fibers to be maturing striated muscle. We feel that the development of this technique may make autogenous **myoblast** transfer therapy a useful treatment for congenital ptosis and other focal myopathies.

20/3,AB/36 (Item 36 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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07516160 93218720

Repair of demyelinated lesions by transplantation of purified O-2A progenitor cells [see comments]

Groves AK; Barnett SC; Franklin RJ; Crang AJ; Mayer M; Blakemore WF; Noble M

Cellular Neurobiology Laboratory, Ludwig Institute for Cancer Research, London, UK.

Nature (ENGLAND) Apr 1 1993, 362 (6419) p453-5, ISSN 0028-0836

Journal Code: NSC

Comment in Nature 1993 Apr 1;362(6419):414-5

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The transplantation of well defined populations of precursor cells offers a means of repairing damaged tissue and of delivering therapeutic compounds to sites of injury or degeneration. For example, a functional immune system can be reconstituted by transplantation of purified haematopoietic stem cells, and transplanted skeletal **myoblasts** and keratinocytes can participate in the formation of normal tissue in host animals. Cell transplantation in the central nervous system (CNS) has been proposed as a means of correcting neuronal dysfunction in diseases associated with neuronal loss; it might also rectify glial cell dysfunction, with transplanted oligodendrocyte precursor cells eventually allowing repair of demyelinating damage in the CNS. Here we use co-operating growth factors to expand purified populations of oligodendrocyte type-2 astrocyte (O-2A) progenitor cells for several weeks in vitro. When **injected** into demyelinating lesions in spinal cords of adult rats, created in such a way as to preclude host-mediated remyelination, these expanded populations are capable of producing extensive remyelination. In addition, transplantation of O-2A progenitor cells genetically modified to express the bacterial beta-galactosidase gene gives rise to beta-galactosidase-positive oligodendrocytes which remyelinate demyelinated axons within the lesion.

These results offer a viable strategy for the manipulation of neural precursor cells which is compatible with attempts to repair damaged CNS tissue by precursor transplantation.

20/3,AB/42 (Item 42 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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07230100 93096163

Arterial delivery of myoblasts to skeletal muscle.

Neumeyer AM; DiGregorio DM; Brown RH Jr
Neurology Service, Massachusetts General Hospital, Boston 02129.
Neurology (UNITED STATES) Dec 1992, 42 (12) p2258-62, ISSN 0028-3878
Journal Code: NZ0

Languages: ENGLISH

Document type: JOURNAL ARTICLE

One of the major limitations of **myoblast** implantation as a therapy for muscular disease is that multiple injections by intramuscular implantation may be required for widespread delivery of cells. Also, some sites (eg, the diaphragm) are relatively inaccessible to **injection**. As an alternative, we have undertaken intra-arterial administration of **myoblasts**. For these experiments, we used donor cell **myoblasts** from the immortal L6 cell line labeled with lacZ via the beta-gal-at-gal retrovirus. In our model, target rat skeletal muscle (tibialis anterior [TA]) was injured using 0.5 ml of 0.5% bupivacaine and 15 IU of hyaluronidase; saline was **injected** into the contralateral side as a control. We infused 3×10^6 lacZ-positive cells into the abdominal aorta of previously injured, immunosuppressed (cyclosporine A) rats. At 7, 14, and 28 days, TA, liver, heart, lung, and spleen were examined for lacZ staining. In both the injured and control muscles, a few differentiated, lacZ-positive muscle cells were present, both singly and in groups, at each time point. These studies demonstrate that genetically labeled, transformed **myoblasts** may migrate from the arterial circulation to muscle and fuse there to form differentiated muscle cells. It is conceivable that intra-arterial delivery of **myoblasts** may have a role in the therapy of selected diseases of skeletal muscle.

20/3,AB/48 (Item 48 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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07071311 92261663

Human myoblast transplantation: preliminary results of 4 cases.

Huard J; Bouchard JP; Roy R; Malouin F; Dansereau G; Labrecque C; Albert N; Richards CL; Lemieux B; Tremblay JP

Laboratoire de Neurobiologie, Hopital de l'Enfant-Jesus, Quebec, Canada.
Muscle Nerve (UNITED STATES) May 1992, 15 (5) p550-60, ISSN 0148-639X
Journal Code: NN9

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Myoblasts from immunocompatible donors have been transplanted into the muscles (tibialis anterior, biceps brachii, and/or extensor carpi radialis longus) of 4 Duchenne patients in the advanced stages of the disease. Although no immunosuppressive treatment was used, none of the patients showed any clinical signs of rejection such as fever, redness, and inflammation. One patient transiently produced antibodies against the donor **myoblasts** as determined by cytofluorometric analysis. This patient and 2 others were shown to form antibodies against their donor's myotubes. Muscle biopsies of the **injected** tibialis anterior of 4 patients revealed that 80%, 75%, 25%, and 0% of the muscle fibers, respectively, showed some degree of dystrophin immunostaining. The contralateral noninjected muscles of the latter 3 patients did not contain any dystrophin positive fibers, while that of the first patient showed dystrophin expression in 16% of the fibers examined. **Myoblasts** were also **injected** into the extensor carpi radialis longus or the biceps brachii of these patients. A few months subsequent to **injection**, one patient was shown to have a 143% increase of

strength during static wrist extension. This result must be interpreted with caution because a double-blind strength-measuring protocol was not used. Furthermore, we have noted that this change slowly decayed over time. The strength of 2 other patients was increased less remarkably (41% and 51%), while the strength of the fourth patient was unchanged.

20/3,AB/78 (Item 78 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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05920948 88242729

Myoblast-mediated fusion- injection: a new technique for introduction of macromolecules specifically into living skeletal muscle cells.

Matsuda R; Noro N; Ichimura T

Department of Biology, Tokyo Metropolitan University, Japan.

Exp Cell Res (UNITED STATES) Jun 1988, 176 (2) p366-70, ISSN 0014-4827 Journal Code: EPB

Languages: ENGLISH

Document type: JOURNAL ARTICLE

A new technique for the introduction of macromolecules specifically into living skeletal muscle cells has been developed by a modification of the red blood cell ghost-mediated fusion-injection technique [M. Furusawa (1980) Int. Rev. Cytol. 62, 29-67]. Fluorescein-labeled bovine serum albumin (FITC-BSA) was introduced into chicken skeletal muscle **myoblasts** by the human red blood cell-mediated fusion-injection method in the presence of polyethylene glycol. **Myoblasts** loaded with FITC-BSA were then purified by a fluorescence cell sorter and cocultured with myotubes. Specific cell fusion between **myoblasts** and myotubes occurred under normal culture conditions and BSA was successfully introduced into living myotubes. This technique may provide a new method not only for the study of a given macromolecule's function in living muscle cells but also for therapeutic purposes such as muscle-specific drug delivery.

20/3,AB/101 (Item 101 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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03231852 77238992

Regeneration of masseter muscle following lidocaine-induced degeneration. A histochemical study.

Dolwick MF; Bush FM; Seibel HR

Acta Anat (Basel) (SWITZERLAND) 1977, 98 (3) p325-33, ISSN 0001-5180
Journal Code: 09A

Languages: ENGLISH

Document type: JOURNAL ARTICLE

The histoenzymatic characteristics of regenerating myofibers of rat masseter muscle following **injection** of 1% lidocaine, as well as morphometric and histochemical characteristics of the typical myofibers, were investigated. **Myoblasts** appeared initially by day 1 among numerous macrophages within the confines of degenerating myofibers. Myotubes predominated by the 3rd day. Complete regeneration of the muscle occurred by at least 45 days. Phosphorylase activity was absent at day 1 and reappeared by the 5th day when the regenerating myofibers showed slight activity. By the 15th day the myofiber types had partly differentiated; red myofibers were smaller and stained less intensely than the white myofibers. Myotubes stained uniformly for succinic dehydrogenase activity from 3 until 5 days. After 5 days this staining increased gradually. Myofiber types began differentiation by 15 days and were fully differentiated by 45 days. ATPase activity was barely evident by 1-3 days. This activity appeared uniformly low up to 5 days and increased to an intensity comparable with that of the typical myofiber by 15 days. Slight leucine aminopeptidase activity occurred in macrophages 1 day following **injection**. By 3 days this activity appeared in the remaining **myoblasts** and in the myotubes. Some activity was found in the fibroblasts. This staining intensity at 5 days was equal to that of earlier lesions. A trace of this activity was

found at 7 days, and none at 15 days. Glucose-6-phosphate dehydrogenase activity was present in the macrophages by day 1. It increased by 3 days and occurred mainly in **myoblasts** and myotubes. This activity decreased by 5 days, and none was found by 7 days.

20/3,AB/109 (Item 109 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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02408000 77199846

Myogenic cell formation in regenerating rat skeletal muscle injured by mincing. II. An autoradiographic study.

Snow MH

Anat Rec (UNITED STATES) Jun 1977, 188 (2) p201-17, ISSN 0003-276X

Journal Code: 4QM

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Myonuclei and satellite cell nuclei were differentially labelled with 3H-thymidine in uninjured skeletal muscle of young rats and then traced autoradiographically at intervals after mincing the radioactive hindlimb muscles to determine the source of regenerating presumptive **myoblasts**. Labelled nuclei were detected by light microscopic examination of 1-micron thick autoradiographs and identified by electron microscopic examination of an adjacent section. Repeated injections of 3H-thymidine during fetal and neonatal development, followed by a 4- to 5-week maturation period, resulted in labelling of 20% of the myonuclei. Satellite cells were not observed to be labelled in this series. Eight to sixteen hours after mincing, 20% of the pyknotic myonuclei were labelled, whereas none of the regenerating presumptive **myoblasts** appeared labelled. A single injection of 3H-thymidine administered to 18-day-old rats, followed by sacrifice within ten hours, resulted in labelling of 23% of the satellite cell nuclei. Myonuclei were not observed to be labelled in this series. Eight to sixteen hours after mincing, silver grains were detected over both pyknotic and regenerating cell nuclei. These experiments indicate that many satellite cells survive muscle injury and transplantation to become regenerating **myogenic cells** at a time when most, if not all, myonuclei are undergoing pyknosis.

20/3,AB/124 (Item 9 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
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08413280 BIOSIS NO.: 000043109859

MYOBLAST TRANSFER INTO SKELETAL MUSCLE UNRESOLVED QUESTIONS OF NEW MUSCLE FORMATION FROM INJECTED MYOGENIC CELLS

AUTHOR: DIMARIO J X; STOCKDALE F E

AUTHOR ADDRESS: STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305-5306.

JOURNAL: KELLY, A. M. AND H. M. BLAU (ED.). RAVEN PRESS SERIES ON MOLECULAR AND CELLULAR BIOLOGY, VOL. 2. NEUROMUSCULAR DEVELOPMENT AND DISEASE. XXV+374P. RAVEN PRESS: NEW YORK, NEW YORK, USA. ILLUS. ISBN 0-88167-920-8. 0 (0). 1992. 329-340.

20/3,AB/130 (Item 15 from file: 5)
DIALOG(R) File 5:BIOSIS PREVIEWS(R)
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06307175 BIOSIS NO.: 000036010328

MYOBLAST INJECTION TREATMENT FOR MUSCLE WEAKNESS

AUTHOR: LAW P K; GOODWIN T G; LI H J; CHEN M

AUTHOR ADDRESS: DEP. NEUROL., UNIV. TENN. MEMPHIS, MEMPHIS, TENN. 38163, USA.

JOURNAL: 18TH ANNUAL MEETING OF THE SOCIETY FOR NEUROSCIENCE, TORONTO, ONTARIO, CANADA, NOVEMBER 13-18, 1988. SOC NEUROSCI ABSTR 14 (1). 1988. 677.

20/3,AB/131 (Item 16 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

05863088 BIOSIS NO.: 000034086237
MYOBLASTS MEDIATED FUSION INJECTION A NEW TECHNIQUE FOR SPECIFIC
INTRODUCTION OF MACROMOLECULES INTO LIVING MUSCLE CELLS

AUTHOR: MATSUDA R; NORO N; ICHIMURA T
AUTHOR ADDRESS: DEP. BIOL., TOKYO METROP. UNIV., TOKYO, JPN.

JOURNAL: SELECTED ABSTRACTS FROM THE 20TH ANNUAL MEETING OF THE JAPANESE SOCIETY OF DEVELOPMENTAL BIOLOGISTS, KYOTO, JAPAN, MAY 28-30, 1987. DEV GROWTH & DIFFER 29 (4). 1987. 409.

20/3,AB/154 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

03688177 Genuine Article#: PW987 Number of References: 20
Title: **WHOLE-BODY MYOBLAST TRANSFER**
Author(s): LAW P; GOODWIN T; FANG Q; DEERING M; DUGGIRALA V; LARKIN C;
FLORENDO A; QUINLEY T; CORNETT J; SHIRZAD A; YOO T; HOLCOMB R
Corporate Source: CELL THERAPY RES FDN,1770 MORIAH WOODS BLVD,SUITE
18/MEMPHIS//TN/38117
Journal: TRANSPLANTATION PROCEEDINGS, 1994, V26, N6 (DEC), P3381-3383
ISSN: 0041-1345
Language: ENGLISH Document Type: ARTICLE

20/3,AB/156 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

03626042 Genuine Article#: PT946 Number of References: 31
Title: **SKELETAL-MUSCLE AS A TARGET FOR GENE-THERAPY**
Author(s): PARTRIDGE T
Corporate Source: CHARING CROSS & WESTMINSTER MED SCH,FULHAM PALACE
RD/LONDON W6 8RF//ENGLAND/
Journal: GENE THERAPY, 1994, V1, N2 (MAR), P77-79
ISSN: 0969-7128
Language: ENGLISH Document Type: EDITORIAL

20/3,AB/173 (Item 21 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02679883 Genuine Article#: LV687 Number of References: 29
Title: **IMPLANTED MYOBLASTS NOT ONLY FUSE WITH MYOFIBERS BUT ALSO SURVIVE AS MUSCLE PRECURSOR CELLS**
Author(s): YAO SN; KURACHI K
Corporate Source: UNIV MICHIGAN,SCH MED,DEPT HUMAN GENET/ANN
ARBOR//MI/48109; UNIV MICHIGAN,SCH MED,DEPT HUMAN GENET/ANN
ARBOR//MI/48109
Journal: JOURNAL OF CELL SCIENCE, 1993, V105, AUG (AUG), P957-963
ISSN: 0021-9533
Language: ENGLISH Document Type: ARTICLE
Abstract: Intramuscular implanted **myoblasts** can fuse with existing myofibers. Here we report that implanted primary **myoblasts** marked

with retroviral transgenes can also persist as muscle precursor cells. These cells can be recovered as viable **myoblasts** from muscles of recipient mice even months after **myoblast** implantation, and they can fully resume expression of the transgenes in culture. Upon re-implantation into muscles, they again not only fuse with existing myofibers, but also survive as muscle precursor cells in the tissue. These reserve **myogenic cells** should be able to contribute to host myofibers in muscle regeneration when the recombinant myofibers are damaged, providing an additional mechanism to maintain a persistent expression of transgenes delivered by **myoblast** -mediated gene transfer.

20/3,AB/189 (Item 37 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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02354320 Genuine Article#: KW449 Number of References: 44
Title: MYOBLAST TRANSPLANTATION - WHATS GOING ON
Author(s): HOFFMAN EP
Corporate Source: UNIV PITTSBURGH,SCH MED,DEPT MOLEC GENET &
BIOCHEM/PITTSBURGH//PA/15261; UNIV PITTSBURGH,SCH MED,DEPT HUMAN
GENET/PITTSBURGH//PA/15261; UNIV PITTSBURGH,SCH MED,DEPT
PEDIAT/PITTSBURGH//PA/15261
Journal: CELL TRANSPLANTATION, 1993, V2, N1 (JAN-FEB), P49-57
ISSN: 0963-6897
Language: ENGLISH Document Type: ARTICLE
Abstract: Muscle tissue, due to its syncytial cellular structure and specific nerve and vascular requirements, cannot be transplanted as an organ. In an effort to use transplantation to overcome genetically determined biochemical deficiencies in muscle, attention has focused on delivering the developmental precursors of mature muscle fibers, **myoblasts**, as donor cells for cellular transplantation. Consequent to a brief report showing limited success of the technique in mice in 1988, human trials were summarily designed, funded, and initiated. The human trials have spurred more controversy than concrete data, with more reports appearing in the popular press than in scientific journals. This review summarizes the events leading to the current state of affairs, and underscores the biological hurdles facing **myoblast** transplantation before it can be considered a therapeutic modality.

20/3,AB/206 (Item 54 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
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01938922 Genuine Article#: JN144 Number of References: 32
Title: FORMATION OF SKELETAL-MUSCLE INVIVO FROM THE MOUSE C2-CELL LINE
Author(s): MORGAN JE; MOORE SE; WALSH FS; PARTRIDGE TA
Corporate Source: CHARING CROSS & WESTMINSTER MED SCH,DEPT HISTOPATHOL,ST
DUNSTONS RD/LONDON W6 8RF//ENGLAND/; UNITED MED & DENT SCH,GUYS
HOSP,DEPT EXPTL PATHOL/LONDON SE1 9RT//ENGLAND/
Journal: JOURNAL OF CELL SCIENCE, 1992, V102, AUG (AUG), P779&
ISSN: 0021-9533
Language: ENGLISH Document Type: ARTICLE
Abstract: The C2 muscle cell line is myogenic in vitro and has been extensively used in studies of muscle cell differentiation. Here, we have investigated the myogenicity in vivo of C2 cells implanted into suitable sites in the mouse.

Large amounts of new muscle were formed when C2 cells were implanted into sites in nude mice which were undergoing regeneration following whole muscle grafting and in scaffolding of freeze-killed muscle or vicryl suture in the anterior tibial compartment. When implanted into regenerating muscle, C2 cells fused with the host muscle to form mosaic fibres; when implanted into inert sites, they formed

muscle of largely donor origin. C2-derived muscle fibres appeared to become innervated, but the progression of N-CAM (neural cell adhesion molecule) isoform changes in such regenerates indicated that they did not become fully mature. Proliferating, undifferentiated cells of C2 origin form tumours in older grafts; however, this was more pronounced in the absence of competition from host muscle cells.

In the short term, C2 cells can form large amounts of muscle in vivo for biochemical analysis. In addition, C2 cells are easily manipulable in vitro; genes of interest may be transfected into them prior to implantation of the cells into skeletal muscle and the effects of these genes in vivo may thus be examined.

20/3,AB/228 (Item 76 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 1998 Inst for Sci Info. All rts. reserv.

01079792 Genuine Article#: FT980 Number of References: 34
Title: DELIVERY SYSTEMS FOR GENE-THERAPY
Author(s): WU GY; WU CH
Corporate Source: UNIV CONNECTICUT, SCH MED, DEPT MED, DIV GASTROENTEROL LIVER
DIS/FARMINGTON//CT/06032
Journal: BIOTHERAPY, 1991, V3, N1, P87-95
Language: ENGLISH Document Type: ARTICLE
Abstract: Introduction of foreign genes into mammalian cells in vitro has been accomplished previously by a variety of methods. The few techniques that have been developed for transfection of mammalian cells in vivo, are technically difficult or lack cell specificity.

We have developed a soluble, targetable DNA carrier system consisting of an asialoglycoprotein covalently coupled to a polycation. The strategy was based on: 1) the presence of unique receptors on hepatocytes which internalize galactose-terminal (asialo-)glycoproteins; 2) polycations can bind DNA in a non-covalent, non-damaging interaction. Using chloramphenicol acetyltransferase (CAT) as a marker gene, specific delivery and expression of CAT was demonstrated in vitro using asialoglycoprotein receptor (+) and (-) cell lines.

Intravenous **injection** of conjugate-DNA complexes in rats resulted in detection of CAT DNA sequences in liver 10 min later by dot blots with a CAT cDNA probe. CAT enzyme activity 24 hrs later was found specifically in liver but no other tissues or control livers. Targeted hepatic CAT expression was transient, maximal at 24 hrs but declined to barely detectable levels by 96 hrs. Persistent foreign gene expression was achieved by **injection** of DNA complex followed by 67% partial hepatectomy. High levels of hepatic CAT activity were detected through 11 weeks post-hepatectomy.

The data indicate that a targetable gene delivery system can permit in vivo expression of an exogenous gene after simple intravenous **injection**. The foreign gene expression can be enhanced and made to persist by induction of hepatocyte replication.

20/3,AB/256 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE
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888095 EMBASE No: 78054506
Regeneration of the skeletal musculature
REGENERATION DER SKELETTMUSKULATUR
Schmalbruch H.
Inst. Neuropsychiol., Univ. Copenhagen DENMARK
VERH.ANAT.GES. (JENA) (GERMANY, EAST) , 1976, Vol.70 II (691-701)
CODEN: VHAGA
LANGUAGES: GERMAN

A new model to study muscle fibre regeneration is presented. Local **injection** of warm (60 to 70degr.C) Ringer solution caused necrosis of most fibres in the soleus muscle of rats but left the endomysium grossly intact. After 1 day in the persisting basement membrane tubes of necrotic fibres **myoblasts** probably derived from satellite cells occurred. Within a few days they fused to bundles of myotubes. After 2 wk numerous new muscle fibres which varied largely in size had been formed. They were arranged in groups enclosed by connective tissue and appeared as fragments of 'split' muscle fibres. This change in architecture which is typical for myopathic muscles is due to focal regeneration in a persisting endomysium. Bundles of myotubes are formed within a common basement membrane; they fuse or become detached and form one or more muscle fibres. Empty meshes of the endomysium condense around foci of regeneration and form a capsule around groups of fibres.

20/3,AB/347 (Item 2 from file: 377)
DIALOG(R)File 377:Derwent Drug File
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00310746 DERWENT ACCESSION NUMBER: 89-03707
Cell Injection Treatment for Muscle Degeneration.
Law P K; Goodwin T G; Li H J; Chen M
Pharmacologist 30, No. 3, A133, 1988

ABSTRACT:

A treatment has been developed to prevent hindlimb and intercostal muscle weakness in murine dystrophy. **Injection** of histoincompatible normal **myoblasts** into dystrophic intercostal and leg muscles improved the structure and function of the muscles to almost normal. Immunosuppression of the C57BL/6J-dy2Jdy2J hosts was by daily s.c. cyclosporin-A. **Injected** dystrophic muscles exhibited greater cross-sectional area, total fiber number, wet weight, and twitch and tetanus tensions 6 mth post-operatively. Fiber typing was more defined and they contained more normal-appearing and less abnormal-appearing fibers than non-**injected** controls. 11/19 Mice that received **myoblast** injections on both sides showed such behavioral improvement that their locomotive patterns were indistinguishable from normal. (congress abstract).

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